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EXAMINER	
COPPINS, JANET L	

ART UNIT	PAPER NUMBER
1625	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/049,381	Applicant(s) DELFOURNE ET AL.	
	Examiner Janet Coppins	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *14* is/are allowed.

6)☒ Claim(s) *1-10, 12, 13* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-14 pending in the instant application.

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-2 (in part), 3-7, 8-12 (in part), 13, and 14, drawn to compounds, compositions, and methods according to Formula I and Ia wherein X=O, in Paper No. 6 is acknowledged, as well as Applicant's provisional election of species of Example 9.

2. Applicants have traversed the Lack of Unity determination, on the following grounds:

(a) Applicants argue that the Office has not provided any reason to support a conclusion of a lack of unity of invention between Groups I and II. Applicants argue that the Office has not considered the criteria for restriction concerning unity of invention. Applicants further argue that the Office has not alleged that the claimed invention, when considered as a whole, lacks technical features that define a contribution over the prior art. The Office has neither alleged nor explained why the claims lack unity of invention nor described the unique special technical feature in each group. Applicants also argue that the Office has not applied any citation of relevant art relating to the "special technical feature" determination under the Patent Cooperation Treaty.

Applicants' arguments have been considered but have not been found persuasive. The Examiner disagrees that the Office has neither alleged or explained why the claims lack unity of invention, nor described the special technical feature. These were discussed in the previous Office Action. Group I is directed to compounds, compositions, and methods according to formulae (I) and (Ia) wherein X=O. As stated above, the compounds of formulae (I) and (Ia)

lack unity of invention. The special technical feature was identified in the previous Office Action, as the tetracyclo ring system ascididemin. A significant structural element, shared by all of the alternatives, which is novel over the prior art, is not present in the compounds of formula (I) or (Ia). An ascididemin structure, identified as the special technical feature, is not a significant structural element that defines a contribution over the prior art. Even if the variable X were considered part of the special technical feature, a lack of unity would still exist because an oxo substituent (X is oxygen) does not have the same significant structural element as an amino or nitroxy substituent (X is NH or N-OH). Regarding the definition of "special technical feature" in PCT Rule 13.2, Applicants argue that a citation of a reference disclosing the technical feature was not provided. The Examiner would like to direct the Applicants' attention to Schmitz et al, *Pure and Applied Chemistry*, page 1395, which teaches several compounds containing the ascididemin core structure, namely alkaloid compounds 2, 3, 7, and 7', and Scheme I compounds leptoclinidinone, I, and II. Therefore, the unity of invention is still considered to be lacking.

The Examiner also disagrees that the Office has not applied any language or reasons or requirements relating to the standard for restriction under the Patent Cooperation Treaty. The claims lacked unity of invention because the claims do not have a common structural feature that defines a contribution over the prior art. Each of the groups set forth in the previous Office Action represents a discrete heterocyclic ring system, in which one skilled in the art, beside which sharing no significant structural element, cannot be said to belong to a recognized class of chemical compounds. Accordingly, the unity of invention is considered to be lacking and restriction of the invention in accordance with the rules of unity of invention is considered to be proper.

(b) Applicants argue that the International Preliminary Examination Report did not raise the issue of lack of unity of invention. Therefore, Applicants argue that when the International Preliminary Examining Authority does not hold that a lack of unity exists, the Office should provide a compelling reason to support a finding of lack of unity of invention at the national stage. In response, it is proper to indicate a Lack of Unity in the national phase, although a lack of unity was not indicated in the PCT phase, as long as the rules of Lack of Unity are followed. The reasons for indicating a lack of unity have been discussed above.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-2 (in part) and 8-12 (in part), drawn to compounds, compositions, and methods according to Formulae (I) and (Ia), wherein X is –NH or –N-OH, withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 6.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Objections

5. Claim 11 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an agent for treating certain strains of human cancer cell lines *in vitro* utilizing a compound according to claim 1, does not reasonably provide enablement for an agent for treating all cancers. In In re Wands, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

8. In the instant case, applicants are claiming a process for "treating patients having a cancer tumor" by administering an effective amount of a compound according to claim 1. Yet the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. For example, the cancer therapy art remains highly unpredictable. Currently, over 3000 different types of cancer exist. The various types of cancers have different causative agents, involve different cellular mechanisms, and, consequently, differ in treatment protocol. The nature of

cancer in the pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face. The instant specification does not give any guidance as to the full range of cancers or cancer tumors that could be treated using the instant claimed process. In order to practice the claimed invention, one skilled in the art would have speculate which cancer could be treated or prevented using the ascididemin derivatives found in the instant claims. The number of possible cancers embraced by the claims would impose undue experimentation on the skilled art worker. Therefore, the broad terminology "A process for treating patients having a cancer tumor" is not enabled because the metes and bounds of the cancers or tumors that could be treated using the ascididemin derivatives found in the instant claims cannot be ascertained. Based on the unpredictable nature of the invention and state of the prior art and the extreme breadth of the claims, one skilled in the art could not use the claimed invention without undue experimentation.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 6 and 7 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility. The aforementioned claims are directed to nonstatutory subject matter. Claims 6 and 7 are drafted in terms of "use",

however "use" is not one of the statutory classes of invention. Clinical Products v. Brenner, 149 USPQ 475, 476 (1966). Accordingly, the claims have not been further treated on the merits.

Claims 6 and 7 also rejected under 35 U.S.C. 112, first paragraph (please see In re Wands, stated above). Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

12. Claims 1-10 rejected under 35 U.S.C. 102(b) as being anticipated by Schmitz, Francis J. et al, *Pure and Applied Chemistry*. Schmitz et al teach polycyclic aromatic alkaloids, isolated from marine organisms, according to formula 7' on page 1395, which read on compounds of the instantly claimed general Formula Ia The above claims, as written, do not exclude compounds according to Formula Ia wherein X=O, R_1, R_2, R_3, R_4, R_6, R_7=H, and R_5 =OH. Schmitz et al also teach the cytotoxicity of the aforementioned compounds.

13. Claim 13 rejected under 35 U.S.C. 102(b) as being anticipated by Bracher, F., *Pharmazie*. Bracher et al teach new anticancer drugs derived from marine organisms, including processes for preparing compounds according to formulae 4a and 4b on page 59, which read on the instantly

claimed process for preparing compounds of general Formula I. Bracher et al disclose a reaction scheme on page 59 that teaches the same intermediates and method steps as the instant claim 13.

Allowable Subject Matter

14. Claim 14 has been searched and is currently allowable over the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet Coppins whose telephone number is 703.308.4422. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on 703.308.4698. The fax phone numbers for the organization where this application or proceeding is assigned are 703.746.9037 for regular communications and 703.872.9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.1235.

Alan L. Rotman

Janet L. Coppins
May 16, 2003

ALAN L. ROTMAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600